FACSIMILE

DRAFT

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NUMBER OF PAGES: seven (including this cover sheet)

December 16, 1998 **INFORMAL COMMUNICATION FOR DISCUSSION ONLY**

Examiner Mary Tung
Group 1644; Biotechnology
U.S. Patent and Trademark Office

re: U.S.S.N. 08/989,362; Gorman and Mattson on MAMMALIAN CELL SURFACE ANTIG ...

Dear Examiner Tung:

The following would be the proposed substance of proposed changes in the claims. I would like to address two administrative issues up front. First, I would like to have the Restriction Requirement reconsidered and made final. This will assure that the determination cannot be later challenged in court to argue double patenting for divisional filings. Secondly, I wanted to ensure that there is no misunderstanding as to the stringency of hybridization. Higher temperatures tend to melt mismatchs in complementary sequences, and high temperature will melt all but the highest matching. Likewise, low salt concentrations will result in mismatches coming apart. Thus, at a given temperature, high salt will tend to maintain complementarity with mismatches, while lower salt (or dilution) will tend to allow such mismatches to come apart. Thus, we believe that the recited conditions in Claims 15 and 16 are actually reasonably high stringency (combination of higher temperature and lower salt).

Please cancel Claims 7-10, 17, and 18-20.
Please amend claims 1-6, 11, and 14-16 as follows:

1. A composition of matter selected from the group consisting of:
   a) a substantially pure or recombinant 499E9 [protein or peptide] polypeptide exhibiting [at least about 85%] 100% sequence identity over a length of at least [about] 12 contiguous amino acids to SEQ ID NO: 2;
   b) a natural sequence 499E9 of SEQ ID NO: 2; or
   c) a fusion protein comprising 499E9 sequence.

2. [A substantially pure or isolated protein comprising a segment exhibiting sequence identity to a corresponding portion of a] The recombinant 499E9 polypeptide of Claim 1, wherein [:
   a) said homology is at least about 90% identity and said portion is at least about 9 amino acids;
   b) said homology is at least about 80% identity and] said [portion] sequence identity is over at least [about] 17 contiguous amino acids[; or
   c) said homology is at least about 70% identity and said portion is at least about 25 amino acids].

3. The composition of matter of Claim 1, wherein said:
   a) 499E9 comprises a mature sequence of Table 1 (see SEQ ID NO: 1) ; or
   b) protein or peptide [:
      i)] is from a [warm blooded animal selected from a] mammal [, including a rodent;
      ii) comprises at least one polypeptide segment of SEQ ID NO: 2;
      iii) exhibits a plurality of portions exhibiting said identity;
      iv) is a natural allelic variant of 499E9;
      v) has a length at least about 30 amino acids;

vi) exhibits at least two non-overlapping epitopes which are specific for a mammalian 499E9;
vii) exhibits a sequence identity at least about 90% over a length of at least about 20 amino acids to a rodent 499E9;
viii) exhibits at least two non-overlapping epitopes which are specific for a rodent 499E9;
ix) exhibits a sequence identity at least about 90% over a length of at least about 20 amino acids to a rodent 499E9;
x) is glycosylated;
xi) is a synthetic polypeptide;
xii) is attached to a solid substrate;
xiii) is conjugated to another chemical moiety;
xiv) is a 5-fold or less substitution from natural sequence; or
xv) is a deletion or insertion variant from a natural sequence].

4. A composition of matter of Claim 1 which is sterile [comprising :
a) a sterile 499E9 protein or peptide of Claim 1; or
b) said 499E9 protein or peptide of Claim 1 and a carrier, wherein said carrier is:
i) an aqueous compound, including water, saline, and/or buffer; and/or
ii) formulated for oral, rectal, nasal, topical, or parenteral administration].

5. The fusion protein of Claim 1, comprising:
a) mature protein comprising sequence of Table 1 (see SEQ ID NO: 2);
b) a detection or purification tag, including a FLAG, His6, or Ig sequence; or
c) sequence of another [TNF] tumor necrosis factor ligand protein.

6. A kit comprising a [protein or polypeptide of Claim 1, and:
a) a] compartment comprising said [protein or] polypeptide of Claim 1 [; and/or
b)] and instructions for use or disposal of reagents in said kit.

11. An isolated or recombinant nucleic acid encoding a [protein or peptide] polypeptide or fusion protein of Claim 1, wherein [:
a)] said 499E9 protein is from a mammal [, including a rodent; or
b) said nucleic acid:
i) encodes an antigenic peptide sequence of Table 1;
ii) encodes a plurality of antigenic peptide sequences of Table 1;
iii) exhibits at least about 80% identity to a natural cDNA encoding said segment;
iv) is an expression vector;
v) further comprises an origin of replication;
vi) is from a natural source;
vii) comprises a detectable label;
viii) comprises synthetic nucleotide sequence;
ix) is less than 6 kb, preferably less than 3 kb;
x) is from a mammal, including a rodent;
xi) comprises a natural full length coding sequence;
xii) is a hybridization probe for a gene encoding said TNF-ligand family protein; or
xiii) is a PCR primer, PCR product, or mutagenesis primer].

14. A kit comprising [said nucleic acid of Claim 11, and:
a)] a compartment comprising said nucleic acid of Claim 11 [;
b) a compartment further comprising a 499E9 protein or polypeptide; and/or
c)] and instructions for use or disposal of reagents in said kit.

15. A nucleic acid which [:
a)] selectively hybridizes under wash conditions of [30] at least 45° C and less than [2M] 500 mM salt to SEQ ID NO: 1[; or
b) exhibits at least about 85% identity over a stretch of at least about 30

16. The nucleic acid of Claim 15, wherein:
a) said wash conditions are at [45] least 55° C [and/or 500] and less than 150 mM salt; or
b) said [identity is at least 90% and/or said stretch is] nucleic acid comprises at least [55] 30 contiguous nucleotides of the coding portion of SEQ ID NO: 1.

[17. The nucleic acid of Claim 16, wherein:
a) said wash conditions are at 55° C and/or 150 mM salt; or
b) said identity is at least 95% and/or said stretch is at least 75 nucleotides.]

Please add new Claims 21-46 as follows:

21. The composition of matter of Claim 1, which comprises the natural sequence 499E9 of SEQ ID NO: 2. OK

22. The recombinant 499E9 polypeptide of Claim 2, wherein said identity is over at least 25 contiguous amino acids. Doesn't make sense, cl 2 is to 17 aa

23. The substantially pure 499E9 polypeptide of Claim 2, wherein said identity is over at least 30 contiguous amino acids.

24. The substantially pure 499E9 polypeptide of Claim 1, which has a length of at least 30 amino acids. ~~OK - Orig cl 3bv~~ Doesn't make sense, " or " OK orig cl 3bv.

25. The substantially pure or recombinant 499E9 polypeptide of Claim 1, which is:
a) glycosylated;
b) a synthetic polypeptide;
c) attached to a solid substrate; or
d) conjugated to another chemical entity. OK

26. A composition comprising said 499E9 polypeptide of Claim 1 and an aqueous carrier. OK

27. The composition of Claim 26, formulated for oral, rectal, nasal, topical, or parenteral administration. OK

28. The nucleic acid of Claim 11, which comprises at least 22 contiguous nucleotides of the coding portion of SEQ ID NO: 1. OK p29

29. An isolated or recombinant nucleic acid which encodes a polypeptide or fusion protein of Claim 1, wherein said polypeptide is an antigenic peptide of Table 1 (see SEQ ID NO: 2). New matter? 11/12

30. The nucleic acid of Claim 29, which comprises at least 29 contiguous nucleotides of the coding portion of SEQ ID NO: 1. p29 OK

31. An isolated or recombinant nucleic acid encoding a polypeptide of Claim 1, which exhibits 100% identity to a natural cDNA encoding said segment. Over the entire length 112/2

32. A vector which encodes a 499E9 polypeptide of Claim 1 and comprises:
a) at least 35 contiguous nucleotides of the coding portion of SEQ ID NO: 1;
b) transcriptional regulatory sequences operably linked to said 499E9 coding sequence; or p32
c) an origin of replication.

33. The vector of Claim 32, comprising at least 41 contiguous nucleotides from the coding portion of SEQ ID NO: 1. p29

34. An isolated or recombinant nucleic acid encoding a polypeptide or fusion protein of Claim 1, wherein said nucleic acid: OK
a) is from a natural source;
b) comprises a detectable label;
c) comprises synthetic nucleotide sequence; or
d) comprises natural full length coding sequence.

35. An isolated or recombinant nucleic encoding a polypeptide of Claim 1, which is a hybridization probe for a gene encoding a tumor necrosis factor ligand family protein. OK

36. A cell comprising said nucleic acid of Claim 29. ? Dep on 29.

37. A cell comprising said nucleic acid of Claim 31. OK pending Δ in 31

38. A cell comprising said nucleic acid of Claim 32. OK

39. A cell comprising said nucleic acid of Claim 34. OK

40. A kit comprising a compartment comprising a nucleic acid of Claim 34 and instructions for use or disposal of reagents in said kit. OK

41. A kit comprising a compartment comprising said nucleic acid of Claim 35 and instructions for use or disposal of reagents in said kit. OK

42. A method of making a protein, comprising culturing a cell of Claim 12 in an environment resulting in expressing said protein. and recovering said protein.

43. A method of making a protein, comprising culturing a cell of Claim 29 in an environment resulting in expressing said protein. and recovering said protein.

44. A method of making a protein, comprising culturing a cell of Claim 32 in an environment resulting in expressing said protein. and recovering said protein.

45. A method of making a duplex nucleic acid comprising contacting a nucleic acid of Claim 29 with a complementary nucleic acid under selective hybridization conditions of at least 45° C and less than 500 mM salt, thereby forming said duplex.

46. A method of making a polynucleotide of Claim 11, comprising amplifying said polypeptide using PCR amplification methods.

REMARKS

III. The Restriction Requirement

Claims 7-10 and 18-20 are canceled pursuant to the finalized and reconsidered Restriction Requirement. Applicants preserve the right to pursue such subject matter in divisional applications without prejudice.

IV. The Amendments

Please cancel Claim 17.

Claim 1 is amended to incorporate a 100% identity measure and delete the "about". In addition, Applicants amend the language to "polypeptide" and include "contiguous" to remove ambiguity.

New Claim 21 selects one alternative embodiment out of the group in Claim 1.

Claim 2 is amended to incorporate a length of 17 contiguous amino acids. New Claim 22 is directed to the 25 amino acid length from the original Claim 2. New Claim 23 adopts a 30 amino acid length, which finds support, e.g., from 14, line 9.

Claim 3 is amended to delete many of the alternative embodiments. Applicants have inserted reference to SEQ ID NO: 1. The deleted embodiments are included in new Claims 24 (3/b/v) and 25 (3/b/x-xiii).

Claim 4 is amended to the single "sterile" alternative embodiment. New Claims 26 and 27 are directed to other embodiments from Claim 4.

Claim 5 is amended to incorporate reference to SEQ ID NO: 2 and to recite tumor

Claim 6 is amended to delete the alternative and simplify the language.

Claim 11 is amended to delete many of the alternative embodiments. New Claim 28 incorporates a specific length of nucleotide identity, which finds support, e.g., on page 29, line 9. New Claim 29 is derived from Claim 11 (b/i). Likewise, new Claim 30 incorporates a specific length of nucleotide identity, which finds support, e.g., on page 29, line 10. New Claims 31 and 32 are derived from Claim 11 (b/iii and b/iv), with Claim 32 incorporating a specific length of nucleotide identity, which finds support, e.g., on page 29, line 10. Support for the language of "operable linkage" is found, e.g., on page 32, lines 1-18. New Claim 33 incorporates a longer length of identity, which also finds support, e.g., on page 29, line 11. New Claim 34 is derived from Claim 11 (b/vi, b/vii, b/viii, and v/xi). New Claim 35 is derived from Claim 11 (b/xii).

Claims 12 and 13 are unchanged, but new Claims 36-39 are derived from Claim 12, directed to nucleic acids split away from Claim 11.

Claim 14 now is directed to a kit embodiment containing the remaining nucleic acid of Claim 11. New Claims 40-41 are directed to kits comprising the nucleic acid embodiments split out from Claim 11, e.g., of Claims 34 and 35.

New Claims 42-46 are directed to methods of using or making a composition of seemingly allowable subject matter. This rejoinder of methods is directed to: making a protein by culturing cells of Claims 12, 29, or 32 in an environment resulting in expression of various nucleic acids; making a duplex nucleic acid by allowing hybridization to occur under selective conditions; or making a polynucleotide by PCR amplification methods. Support for expressing nucleic acids is found, e.g., in the section beginning on page 31, describing recombinant expression. Support for making duplex nucleic acids is found, e.g., in the section beginning on page 26, describing hybridization, and generally in the references listed on page 44. Support for PCR methods is found, e.g., on page 27, lines 1-13, or in references listed on page 44.

The support for the amendments are described, and Applicants believe no new matter is introduced by the amendments. Applicants had paid claim fees for 3 independent claims, and 20 total claims. The proposed claims number two independent claims and thirty-eight total claims. Applicants authorize charging the DNAX Research Institute Deposit Account 04-1239 for the additional claim fees, e.g., for the additional eighteen claims.

.....

I will call you when I get in on Thursday, probably about 12:30 P.M. your time, to further discuss any remaining issues. Should we be able to resolve issues, I will submit a formal response with these claims as quickly as possible on Thursday. Thank you very much.

Very truly yours:

Edwin P. Ching

following: draft claims

DRAFT CLAIMS FOR DISCUSSION PURPOSES ONLY

1. A composition of matter selected from the group consisting of:
   a) a substantially pure or recombinant 499E9 polypeptide exhibiting 100% sequence identity over a length of at least 12 contiguous amino acids to SEQ ID NO: 2;
   b) a natural sequence 499E9 of SEQ ID NO: 2; or
   c) a fusion protein comprising 499E9 sequence.

2. The recombinant 499E9 polypeptide of Claim 1, wherein said sequence identity is over at least 17 contiguous amino acids. 100%?

3. The composition of matter of Claim 1, wherein said:
   a) 499E9 comprises a mature sequence of Table 1 (see SEQ ID NO: 1); or
   b) protein or peptide is from a mammal.

4. A composition of matter of Claim 1 which is sterile.

5. ~~The~~ fusion protein of Claim 1, comprising:
   a) mature protein comprising sequence of Table 1 (see SEQ ID NO: 2);
   b) a detection or purification tag, including a FLAG, His6, or Ig sequence; or
   c) sequence of another tumor necrosis factor ligand protein.

6. A kit comprising a compartment comprising said polypeptide of Claim 1 and instructions for use or disposal of reagents in said kit.

11. An isolated or recombinant nucleic acid encoding a polypeptide or fusion protein of Claim 1, wherein said 499E9 protein is from a mammal.

14. A kit comprising a compartment comprising said nucleic acid of Claim 11 and instructions for use or disposal of reagents in said kit.

15. A nucleic acid which selectively hybridizes under wash conditions of at least 45° C and less than 500 mM salt to SEQ ID NO: 1.

16. The nucleic acid of Claim 15, wherein: #30 No so marked
   a) said wash conditions are at least 55° C and less than 150 mM salt; or
   b) said nucleic acid comprises at least 30 contiguous nucleotides of the coding portion of SEQ ID NO: 1.

21. The composition of matter of Claim 1, which comprises the natural sequence 499E9 of SEQ ID NO: 2.

22. The recombinant 499E9 polypeptide of Claim 2, wherein said identity is over at least 25 contiguous amino acids.

23. The substantially pure 499E9 polypeptide of Claim 2, wherein said identity is over at least 30 contiguous amino acids.

24. The substantially pure 499E9 polypeptide of Claim 1, which has a length of at least 30 amino acids.

25. The substantially pure or recombinant 499E9 polypeptide of Claim 1, which is:
   a) glycosylated;
   b) a synthetic polypeptide;
   c) attached to a solid substrate; or
   d) conjugated to another chemical entity.

26. A composition comprising said 499E9 polypeptide of Claim 1 and an aqueous carrier.

27. The composition of Claim 26, formulated for oral, rectal, nasal, topical,

28. The nucleic acid of Claim 11, which comprises at least 22 contiguous nucleotides of the coding portion of SEQ ID NO: 1. p29

29. An isolated or recombinant nucleic acid which encodes a polypeptide or fusion protein of Claim 1, wherein said polypeptide is an antigenic peptide of Table 1 (see SEQ ID NO: 2).

30. The nucleic acid of Claim 29, which comprises at least 29 contiguous nucleotides of the coding portion of SEQ ID NO: 1. p29

31. An isolated or recombinant nucleic acid encoding a polypeptide of Claim 1, which exhibits 100% identity to a natural cDNA encoding said segment.

32. A vector which encodes a 499E9 polypeptide of Claim 1 and comprises:
a) at least 35 contiguous nucleotides of the coding portion of SEQ ID NO: 1; p29
b) transcriptional regulatory sequences operably linked to said 499E9 coding sequence; or
c) an origin of replication.

33. The vector of Claim 32, comprising at least 41 contiguous nucleotides from the coding portion of SEQ ID NO: 1. p29

34. An isolated or recombinant nucleic acid encoding a polypeptide or fusion protein of Claim 1, wherein said nucleic acid:
a) is from a natural source;
b) comprises a detectable label;
c) comprises synthetic nucleotide sequence; or
d) comprises natural full length coding sequence.

35. An isolated or recombinant nucleic encoding a polypeptide of Claim 1, which is a hybridization probe for a gene encoding a tumor necrosis factor ligand family protein.

36. A cell comprising said nucleic acid of Claim 29.

37. A cell comprising said nucleic acid of Claim 31.

38. A cell comprising said nucleic acid of Claim 32.

39. A cell comprising said nucleic acid of Claim 34.

40. A kit comprising a compartment comprising a nucleic acid of Claim 34 and instructions for use or disposal of reagents in said kit.

41. A kit comprising a compartment comprising said nucleic acid of Claim 35 and instructions for use or disposal of reagents in said kit.

42. A method of making a protein, comprising culturing a cell of Claim 12 in an environment resulting in expressing said protein.

43. A method of making a protein, comprising culturing a cell of Claim 29 in an environment resulting in expressing said protein.

44. A method of making a protein, comprising culturing a cell of Claim 32 in an environment resulting in expressing said protein.

45. A method of making a duplex nucleic acid comprising contacting a nucleic acid of Claim 29 with a complementary nucleic acid under selective hybridization conditions of at least 45° C and less than 500 mM salt, thereby forming said duplex.

46. A method of making a polynucleotide of Claim 11, comprising amplifying said polypeptide using PCR amplification methods.

08/989,362

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=> s 499e9

L1 2 499E9

=> d l1 1-2 ibib ab

L1 ANSWER 1 OF 2 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1998:405980 CAPLUS
DOCUMENT NUMBER: 129:80627
TITLE: T cell surface antigen **499E9** of mouse, cDNA encoding **499E9**, and production of **499E9** with recombinant cells
INVENTOR(S): Gorman, Daniel M.; Mattson, Jeanine D.
PATENT ASSIGNEE(S): Schering Corp., USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2

Supplied by inventor

PATENT INFORMATION:	NUMBER	DATE
	WO 9825958 A2	19980618

DESIGNATED STATES: W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG

APPLICATION INFORMATION: WO 97-US22766 19971212
PRIORITY APPLN. INFO.: US 96-32846 19961213
DOCUMENT TYPE: Patent
LANGUAGE: English

AB CDNA encoding a T cell surface antigen from mouse, reagents related thereto including purified proteins, specific antibodies, and nucleic acids encoding this antigen are provided. Methods of using said reagents and diagnostic kits are also provided. The cDNA for protein **499E9**, which is expressed on the surface of highly polarized mouse Th1 T cells, was cloned and sequenced. The 316-amino acid protein is a type II transmembrane protein which exhibits structural motifs characteristic of a member of the TNF ligand family. Transcript anal. identified multiple transcripts with the most prevalent being 2.1-2.3 kb. Southern anal. indicated **499E9** is produced in many T cells although pos. signals were also found in brain, heart, kidney, liver, lung, spleen and testis.

L1 ANSWER 2 OF 2 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD
ACCESSION NUMBER: 98-348452 [30] WPIDS
DOC. NO. CPI: C98-107753
TITLE: Mouse cell surface antigen, **499E9** protein - used to treat conditions associated with abnormal physiology or development.
DERWENT CLASS: B04 D16
INVENTOR(S): GORMAN, D M; MATTSON, J D
PATENT ASSIGNEE(S): (SCHE) SCHERING CORP
COUNTRY COUNT: 78
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9825958	A2	980618 (9830)*		EN	58

RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AU AZ BA BB BG BR BY CA CN CZ EE GE GW HU ID IL IS JP KG KR KZ LC LK LR LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK SL TJ TM TR TT UA UZ VN YU

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9825958	A2	WO 97-US22766	971212

PRIORITY APPLN. INFO: US 96-32846 961213

AB WO 9825958 A UPAB: 980730
A substantially pure or recombinant polypeptide (A) exhibiting at least 85% sequence identity over a length of at least 12 amino acids to the 316 amino acid sequence of the mouse **499E9** protein given in the specification, is new.

Also claimed are: (1) a fusion protein comprising (A); (2) an isolated nucleic acid which encodes (A) or the fusion protein of (1); (3) an isolated nucleic acid having the 2191 bp cDNA sequence encoding mouse **499E9** given in the specification; (4) a nucleic acid which hybridises under wash conditions of 30 deg. C and less than 2 M salt to the 2191 bp cDNA sequence, or which exhibits at least 85% identity over 30 nucleotides to a nucleic acid encoding a **499E9** polypeptide; (5) a recombinant vector comprising the nucleic acid of (3) or (4); (6) a host cell comprising the vector of (5), or the nucleic acid of (3) or (4); (7) a binding compound comprising an antibody or antigen binding fragment which specifically binds to (A); and (8) a composition comprising (A) or the fusion protein of (1).

USE - The **499E9** protein is expressed highly on

polarised Th1 T cells, binding of **499E9** to its receptor may result in either immune cell expansion or apoptosis. Antagonists of **499E9** may be used to modulate immune responses in abnormal situations, e.g. autoimmune disorders including rheumatoid arthritis, systemic lupus erythematosus, Hashimoto's autoimmune thyroiditis, as well as acute inflammatory responses in which T-cell expansion, activation or immunological T-cell memory play an important role. The host cell of (6) can be used to produce (A) or the fusion protein (claimed). The antibodies can be used to raise anti-idiotypic antibodies which will be useful in detecting or diagnosing various immunological conditions related to the expression of antigens of **499E9**. The antibodies, and fragments of **499E9** can be used in the treatment of conditions associated with abnormal physiology or development, including abnormal proliferation (e.g. cancerous conditions) or degenerative conditions.

Dwg.0/0

=> s (tnf or tumor(w)necrosis(w)factor)

L2 222656 (TNF OR TUMOR(W) NECROSIS(W) FACTOR)

=> s l2 and (apoptosis or programmed(w)cell(w)death)

L3 10817 L2 AND (APOPTOSIS OR PROGRAMMED(W) CELL(W) DEATH)

=> s l3 and ligand

6 FILES SEARCHED...

1973 L3 AND LIGAND

=> s l4 and th1(4a)cell

L5 23 L4 AND TH1(4A) CELL

=> dup rem

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L6 10 DUP REM L5 (13 DUPLICATES REMOVED)

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L6 ANSWER 1 OF 10 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 1

ACCESSION NUMBER: 1998:394848 CAPLUS

Correction of: 1998:77785

DOCUMENT NUMBER: 129:15139

Correction of: 128:179114

TITLE: Selective induction of **apoptosis** in mature T lymphocytes by variant T cell receptor **ligands**

AUTHOR(S): Combadiere, Behazine; Reis e Sousa, Caetano; Germain, Ronald N.; Lenardo, Michael J.

CORPORATE SOURCE: Mol. Dev. Immune System Sect., Lab. Immunology, Natl. Inst. Allergy and Infectious Dis., Natl. Inst. Health, Bethesda, MD, 20892, USA

SOURCE: J. Exp. Med. (1998), 187(3), 349-355

CODEN: JEMEAV; ISSN: 0022-1007

PUBLISHER: Rockefeller University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Activation, anergy, and **apoptosis** are all possible outcomes of T cell receptor (TCR) engagement. The first leads to proliferation and effector function, whereas the others can lead to partial or complete immunol. tolerance. Structural variants of immunizing peptide-major histocompatibility complex mol. **ligands** that induce selective lymphokine secretion or anergy in mature T cells in assocn. with altered intracellular signaling events have been described. Here the authors describe altered **ligands** for mature mouse CD4+ T helper 1 cells that lead to T cell **apoptosis** by the selective expression of Fas **ligand** (FasL) and **tumor necrosis factor** (TNF) without concomitant IL-2, IL-3, or interferon .gamma. prodn. All **ligands** that stimulated cell death were found to induce FasL and TNF mRNA expression and TCR aggregation ("capping") at the cell surface, but did not elicit a common pattern of tyrosine phosphorylation of the TCR-assocd. signal transduction chains. Thus, TCR **ligands** that uniquely trigger T cell **apoptosis** without inducing cytokines that are normally assocd. with activation can be identified.

L6 ANSWER 2 OF 10 SCISEARCH COPYRIGHT 1998 ISI (R)

ACCESSION NUMBER: 97:217679 SCISEARCH

THE GENUINE ARTICLE: WM435

TITLE: Lack of chronic immune activation in HIV-infected chimpanzees correlates with the resistance of T cells to Fas/Apo-1 (CD95)-induced **apoptosis** and preservation of a T helper 1 phenotype

AUTHOR: Gougeon M L (Reprint); Lecoeur H; Boudet F; Ledru E; Marzabal S; Boullier S; Roue R; Nagata S; Heeney J

CORPORATE SOURCE: INST PASTEUR, UNITE ONCOL VIRALE, DEPT AIDS & RETROVIRUSES, 28 RUE DR ROUX, F-75724 PARIS 15, FRANCE (Reprint); BEGIN MIL HOSP, INFECT DIS SERV, ST MANDE, FRANCE; OSAKA UNIV, SCH MED, DEPT GENET, SUITA, OSAKA 565, JAPAN; BIOMED PRIMATE RES CTR, DEPT VIROL, VIRAL PATHOGENESIS LAB, RIJSWIJK, NETHERLANDS

COUNTRY OF AUTHOR: FRANCE; JAPAN; NETHERLANDS

SOURCE: JOURNAL OF IMMUNOLOGY, (15 MAR 1997) Vol. 158, No. 6, pp. 2964-2976.
Publisher: AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
ISSN: 0022-1767.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: English

REFERENCE COUNT: 64

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Chimpanzees are one of the few species, along with humans, susceptible to persistent HIV-1 infection. However, HIV-infected chimpanzees do not exhibit the marked immune system alterations seen in humans and remain relatively resistant to AIDS. In humans, HIV infection leads to unresponsiveness of T cells in response to TCR stimulation, associated with increased T cell death by **apoptosis**. In an effort to understand some of the mechanisms used to limit lentivirus infection in African nonhuman primates, we compared **apoptosis** in infected humans vs chimpanzees in CD4 and CD8 T cells in relation with the expression of Bcl-2 and Fas molecules. The intensity of **apoptosis** in CD4 and CD8 T cells from infected chimpanzees was very low, was not inducible by several TCR-dependent activators, and was comparable to that detected in noninfected chimpanzees. Moreover, CD45RO(+) and HLA-DR(+) subsets, which were shown to exhibit ex vivo a high propensity to undergo **apoptosis** in infected humans, were not modified in infected chimpanzees. Interestingly, in contrast to

the situation found in infected humans, Fas ligation by agonistic Abs or recombinant human Fas **ligand** on CD4 and CD8 T cells from infected chimpanzees did not induce **apoptosis** in these subsets even when Bcl-2 was down-regulated. Finally, this resistance to **apoptosis** was associated with the predominance of CD3 T **cells** with a **Th1** phenotype. Together these observations argue for a strong relationship among the absence of chronic immune stimulation in HIV-1-infected chimpanzees, the normal control of lymphocyte survival, and the resistance to disease progression.

L6 ANSWER 3 OF 10 SCISEARCH COPYRIGHT 1998 ISI (R)
ACCESSION NUMBER: 97:606839 SCISEARCH
THE GENUINE ARTICLE: XQ080
TITLE: Th1 and Th2 subsets equally undergo Fas-dependent and -independent activation-induced cell death
AUTHOR: Watanabe N; Arase H; Kurasawa K; Iwamoto I; Kayagaki N; Yagita H; Okumura K; Miyatake S; Saito T (Reprint)
CORPORATE SOURCE: CHIBA UNIV, SCH MED, CTR BIOMED SCI, DIV MOL GENET, CHUO KU, 1-8-1 INOHANA, CHIBA 260, JAPAN (Reprint); CHIBA UNIV, SCH MED, CTR BIOMED SCI, DIV MOL GENET, CHUO KU, CHIBA 260, JAPAN; CHIBA UNIV, SCH MED, DEPT INTERNAL MED 2, CHUO KU, CHIBA 260, JAPAN; JUNTENDO UNIV, SCH MED, DEPT IMMUNOL, TOKYO 113, JAPAN
COUNTRY OF AUTHOR: JAPAN
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (AUG 1997) Vol. 27, No. 8, pp. 1858-1864.
Publisher: VCH PUBLISHERS INC, 303 NW 12TH AVE, DEERFIELD BEACH, FL 33442-1788.
ISSN: 0014-2980.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 43
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Stimulation of previously activated T cells results in **apoptosis**, termed activation-induced cell death (AICD). Recent analysis revealed that the Fas/Fas ligand (FasL) interaction is predominantly involved in AICD of T cells. Furthermore, based on the analysis of various T cell clones and lines, it has been reported that FasL is expressed mainly in **Th1** but not in Th2 **cells**. However, the exact expression pattern of Fast and its function in normal activated T cells has not been determined. In the present study, by utilizing completely differentiated **Th1** and Th2 **cell** populations obtained from ovalbumin-specific T cell receptor (TCR)-transgenic mice, the FasL expression on Th1 and Th2 was determined. Furthermore, involvement of Fas-FasL interaction in AICD of **Th1** and Th2 **cells** was analyzed by two approaches: one was the inhibition of AICD by anti-Fast monoclonal antibodies, and the other AICD of Th1/Th2 subsets from TCR-transgenic mice backcrossed to lpr mice. We demonstrated that Th2 cells express FasL on the cell surface at a level similar to that expressed by **Th1 cells**, and that both subsets were equally susceptible to the Fas-mediated AICD. These observations suggest not only that the expression of FasL is not always correlated with Th subsets as defined by the cytokine-producing profile, but also that the responses of both Th1 and Th2 subsets are regulated by Fas-mediated AICD. Finally, analysis of the kinetics of AICD revealed a novel Fas/FasL-independent pathway in its initial stage. These findings revealed the precise function of Fas/ FasL-mediated as well as Fas/FasL-independent AICD in the regulation of helper T cell responses.

L6 ANSWER 4 OF 10 SCISEARCH COPYRIGHT 1998 ISI (R)
ACCESSION NUMBER: 96:712087 SCISEARCH
THE GENUINE ARTICLE: VF753
TITLE: INTRACELLULAR SIGNALING FOR INDUCIBLE ANTIGEN RECEPTOR-MEDIATED FAS RESISTANCE IN B-CELLS
AUTHOR: FOOTE L C; SCHNEIDER T J; FISCHER G M; WANG J K M; RASMUSSEN B; CAMPBELL K A; LYNCH D H; JU S T; MARSHAKROTHSTEIN A; ROTHSTEIN T L (Reprint)
CORPORATE SOURCE: BOSTON UNIV, MED CTR HOSP, ROOM E-556, 88 E NEWTON ST, BOSTON, MA, 02118 (Reprint); BOSTON UNIV, MED CTR, DEPT MICROBIOL, BOSTON, MA, 02118; BOSTON UNIV, MED CTR, DEPT MED, BOSTON, MA, 02118; BOSTON UNIV, MED CTR, DEPT PATHOL, BOSTON, MA, 02118; BOSTON UNIV, MED CTR, EVANS MEM DEPT CLIN RES, BOSTON, MA, 02118; IMMUNEX RES & DEV CORP, DEPT IMMUNOBIOL, SEATTLE, WA, 98101
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF IMMUNOLOGY, (01 SEP 1996) Vol. 157, No. 5, pp. 1878-1885.
ISSN: 0022-1767.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 52
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB CD40 **ligand**-activated B cells are sensitive targets for CD4(+) **Th1** effector **cells** that kill in a Fas-dependent fashion. Susceptibility to **apoptosis** is counteracted by Ag receptor binding that produces a state of resistance to Fas engagement in otherwise sensitive targets. In the present study, protection from Th1-mediated **apoptosis** was found to be induced by protein kinase C and calcium signals, which in combination mimicked the level of Fas resistance produced by surface Ig engagement. Signaling for Fas resistance did not alter Fas expression. Furthermore, B **cells** that were protected against **Th1**-mediated **apoptosis** were also resistant to **apoptosis** mediated by soluble, rFas **ligand**. Taken together, these results indicate that signaling for protection against Fas-mediated **apoptosis** does not depend on alteration of the interaction between B **cell** target and **Th1** effector populations. Instead, surface IgM-derived protein kinase C and calcium signals appear to produce an intracellular change in the Fas signaling pathway that develops over a period of hours and interferes with the apoptotic process through a mechanism that depends on protein synthesis.

L6 ANSWER 5 OF 10 SCISEARCH COPYRIGHT 1998 ISI (R)
ACCESSION NUMBER: 96:735091 SCISEARCH
THE GENUINE ARTICLE: VK663
TITLE: FAS EXPRESSION AND APOPTOSIS IN HUMAN B-CELLS
AUTHOR: SCHATTNER E (Reprint); FRIEDMAN S M
CORPORATE SOURCE: NEW YORK HOSP, DEPT MED, DIV HEMATOL ONCOL, ROOM C-606, 525 E 68TH ST, NEW YORK, NY, 10021 (Reprint); CORNELL UNIV, HOSP SPECIAL SURG, COLL MED, DIV RHEUMATOL, NEW YORK, NY, 10021
COUNTRY OF AUTHOR: USA
SOURCE: IMMUNOLOGIC RESEARCH, (1996) Vol. 15, No. 3, pp. 246-257.

ISSN: 0257-277X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 82

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Mechanisms of B cell **apoptosis** are critical in reducing aberrant B cell proliferations such as those that arise in autoimmune disease and in B cell malignancies. The physiologic interaction of CD4+ helper T cells and B lymphocytes has been extensively studied over the past two decades. Although CD4+ T cells are considered primarily to offer positive costimulatory signals for B cell differentiation into active immunoglobulin-secreting cells, recent studies have shown that CD4+ T cells are crucial in downregulating the humoral immune response. In the course of cognate interaction between CD40 **ligand** (CD40L)-bearing CD4+ T cells and CD40-expressing germinal center B cells, CD40 ligation results in augmented Fas expression at the B cell surface. Like CD40L, Fas **ligand** is expressed on activated CD4+ **Th1 cells** and when bound to Fas receptor on the B cell surface, initiates an apoptotic signal in that cell. Thus, CD4+ T cells limit the growth of autologous germinal center B cells by first inducing Fas expression and then instigating a death signal via Fas **ligand**. In this work, we will consider these observations about CD4+ T-cell-induced, Fas-mediated B cell death in the context of other factors that affect **apoptosis** in B cells, normal and malignant.

L6 ANSWER 6 OF 10 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 97069901 MEDLINE
DOCUMENT NUMBER: 97069901
TITLE: Interferon-gamma-inducing factor, a novel cytokine, enhances Fas **ligand**-mediated cytotoxicity of murine T helper 1 cells.
AUTHOR: Dao T; Ohashi K; Kayano T; Kurimoto M; Okamura H
CORPORATE SOURCE: Fujisaki Institute, Hayashibara Biochemical Laboratories, Inc., Okayama, Japan.
SOURCE: CELLULAR IMMUNOLOGY, (1996 Nov 1) 173 (2) 230-5. Journal code: CQ9. ISSN: 0008-8749.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199702
ENTRY WEEK: 19970204

AB Fas **ligand** (FasL), expressed on activated T cells, plays a central role in regulating the immune response by inducing **apoptosis** in activated lymphocytes through binding to its receptor, Fas. We report here that a newly discovered cytokine, interferon-gamma-inducing factor (IGIF) (H. Okamura et al., Nature 378, 88, 1995), selectively enhances the FasL-mediated cytotoxicity of cloned murine **Th1 cells**, but not Th0 or Th2 cells. Anti-IFN-gamma antibody (Ab) did not block the IGIF-induced cytotoxicity of **Th1 cells**, nor did IFN-alpha, IFN-gamma, or TNF-alpha augment the cytotoxic activity of Th1, thus indicating that this enhanced cytotoxicity of **Th1 cells** was mediated by IGIF. In addition, IL-12 was also found to enhance the FasL-mediated cytotoxicity of **Th1 cells**, suggesting that **Th1 cells** possesses receptors for both cytokines although these cytokines can act via different pathways. The results thus show that IGIF, recently proposed as IL-18, might play a potential role in immunoregulation or in inflammation by augmenting the functional activity of FasL on **Th1 cells**.

L6 ANSWER 7 OF 10 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1998268135 MEDLINE
DOCUMENT NUMBER: 98268135
TITLE: Induction of lymphomonocyte activation by HIV-1 glycoprotein gp120. Possible role in AIDS pathogenesis.
AUTHOR: Capobianchi M R
CORPORATE SOURCE: Institute of Virology, University La Sapienza Roma, Italy.
SOURCE: JOURNAL OF BIOLOGICAL REGULATORS AND HOMEOSTATIC AGENTS, (1996 Oct-Dec) 10 (4) 83-91. Ref: 64
Journal code: 128. ISSN: 0393-974X.
PUB. COUNTRY: Italy
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY WEEK: 19981001

AB Dysfunction of cytokine secretion pattern has been suggested to play a central role in the immunopathogenesis of HIV infection. In fact a shift of T helper cell functions from a **Th1**-type to TH0- or TH2-type has been observed in HIV-1 infected subjects undergoing disease progression. The inhalance of cytokine network is accompanied by persistent activation of the immune system, impaired ability to mount a proper activation response (anergy), and priming to **apoptosis**. Extensive investigation during the last decade has been conducted on the influence of HIV-1 gp120 or of its precursor gp160 on several lymphocyte and monocyte functions. Gp120 is able to rise intracellular calcium concentration and to induce the formation of inositol triphosphate, can block mitogen- or antigen-driven T cell activation, can induce altered cytokine production by activated PBMC subpopulations, determines impaired cytotoxicity and chemotactic response to antigens, interferes with the activity of antigen presenting cells, enhances or induces **apoptosis**, stimulates polyclonal B cell activation and induces or up-modulates a number of cytokines, including IL-6. TNF, IL-1-alpha and -beta, IL-10 and IL-8. Furthermore, both IFN-alpha and -gamma, as well as several markers of IFN activity, such as beta 2-microglobulin and neopterin, are induced in gp120-stimulated PBMC. However, neither IL-4 (Th2-type) nor IL-2 (Th1-type), nor DNA synthesis are activated by gp120. On the other hand gp120-stimulated PBMC express increased IL-2 receptors, and can be induced by exogenous IL-2 to proliferate, suggesting that they are in a state of at least partial activation. According to this hypothesis, other activation markers, both early (such as CD69), and late (such as CD45RO and CD71), are induced by gp120, but this even partial activation does not lead to the ability of PBMC to support productive infection by HIV-1, unless in the presence of exogenous IL-2. The HIV-induced cytokines can influence HIV infection either directly, by up- or down-modulating virus replication, or indirectly, by modulating the expression of cellular molecules. In fact, during the budding process, the HIV envelope captures a number of cell membrane proteins, including cytokine receptors such as IL-2R, adhesion molecules such as LFA-1, ICAM-1, -2, HLA Class I and II, as well as cell lineage markers. Gp120-induced cytokines, particularly IFN-gamma, upmodulate the cellular expression of intercellular adhesion molecules, such as ICAM-1. We have shown that the IFN-gamma-driven increase of the expression of ICAM-1 by cells chronically infected with HIV-1 can be transmitted to the virus progeny, resulting in phenotypic alteration of the virus, and leading to the expansion of its host cell spectrum to CD4-negative

cells expressing the appropriate ligands, i.e. LFA-1. Intercellular adhesion molecules are also involved in the cell-mediated transmission of HIV infection, and the increased ICAM-1 expression induced by IFN-gamma determines a stimulation of the transmission of HIV from abortively infected endothelial cells to permissive CD4 lymphocytes. On the whole, these data indicate that HIV, or its soluble products such as gp120, can modify several PBMC functions, by inducing a number of cytokines and a partial state of immune activation. It is possible that the gp120-driven changes of PBMC functions are not only an epiphenomenon of HIV infection, but rather, it is likely that they can participate in the immunopathological events responsible for disease progression.

L6 ANSWER 8 OF 10 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 4
ACCESSION NUMBER: 96:31518 BIOSIS
DOCUMENT NUMBER: 98603653
TITLE: Th1 CD4+ lymphocytes delete activated macrophages through the Fas-APO-1 antigen pathway.
AUTHOR(S): Ashany D; Song X; Lacy E; Nikolic-Zugic J; Friedman S M; Elkon K B
CORPORATE SOURCE: Hosp. Special Surgery, 535 East 70th Street, New York, NY 10021, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America 92 (24). 1995. 11225-11229. ISSN: 0027-8424
LANGUAGE: English
AB The Fas/APO-1 cytotoxic pathway plays an important role in the regulation of peripheral immunity. Recent evidence indicates that this regulatory function operates through deletion of activated T and B lymphocytes by CD4+ T cells expressing the Fas ligand. Because macrophages play a key role in peripheral immunity, we asked whether Fas was involved in T-cell-macrophage interactions. Two-color flow cytometry revealed that Fas receptor (FasR) was expressed on resting murine peritoneal macrophages. FasR expression was upregulated after activation of macrophages with cytokines or lipopolysaccharide, although only tumor necrosis factor-alpha rendered macrophages sensitive to anti-FasR antibody-mediated death. To determine the consequence of antigen presentation by macrophages to CD4+ T cells, macrophages were pulsed with antigen and then incubated with either Th1 or Th2 cell lines or clones. Th1, but not Th2, T cells induced lysis of 60-80% of normal macrophages, whereas macrophages obtained from mice with mutations in the FasR were totally resistant to Th1-mediated cytotoxicity. Macrophage cytotoxicity depended upon specific antigen recognition by T cells and was major histocompatibility complex restricted. These findings indicate that, in addition to deletion of activated lymphocytes, Fas plays an important role in deletion of activated macrophages after antigen presentation to Th1 CD4+ T cells. Failure to delete macrophages that constitutively present self-antigens may contribute to the expression of autoimmunity in mice deficient in FasR (lpr) or Fas ligand (gld).

L6 ANSWER 9 OF 10 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 95221885 MEDLINE
DOCUMENT NUMBER: 95221885
TITLE: Expression of the Fas ligand in cells of T cell lineage.
AUTHOR: Suda T; Okazaki T; Naito Y; Yokota T; Arai N; Ozaki S; Nakao K; Nagata S
CORPORATE SOURCE: Department of Molecular Biology, Osaka Bioscience Institute, Japan..
SOURCE: JOURNAL OF IMMUNOLOGY, (1995 Apr 15) 154 (8) 3806-13. Journal code: IFB. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199507
AB Fas ligand (FasL) is a membrane-type cytokine belonging to the TNF family, and induces apoptosis through its cell-surface receptor, Fas. To determine the cell types that express FasL, various mouse tissues and cell lines were examined by Northern hybridization using a mouse FasL cDNA as a probe. Among tissues, lymphoid organs (thymus, lymph node, spleen), lung, and small intestine express low levels of FasL mRNA, suggesting the role of FasL in the general immune system and mucosal immunity. The testis expressed FasL mRNA most abundantly; however, the size of FasL mRNA in the testis was slightly shorter than those in other tissues. Distribution of FasL mRNA in a panel of cell lines indicated that the FasL expression is rather restricted to the cells of T cell lineage. Activation of the splenocytes with the T cell activators such as PMA and ionomycin, Con A, anti-CD3, or even IL-2 alone induced the expression of the FasL. CD8+ splenocytes expressed the FasL more abundantly than did the CD4+ splenocytes upon activation by Con A and IL-2. Among CD4+ CTL cell lines, the FasL was expressed in all Th1 and Th0, and some Th2 clones.

L6 ANSWER 10 OF 10 SCISEARCH COPYRIGHT 1998 ISI (R)
ACCESSION NUMBER: 95:690311 SCISEARCH
THE GENUINE ARTICLE: RX342
TITLE: DOWN-MODULATION OF CD4(+) T-HELPER TYPE-2 AND TYPE-0 CELLS BY T-HELPER TYPE-1 CELLS VIA FAS FAS-LIGAND INTERACTION
AUTHOR: HAHN S; STALDER T; WERNLI M; BURGIN D; TSCHOPP J; NAGATA S; ERB P (Reprint)
CORPORATE SOURCE: UNIV BASEL, INST MED MIKROBIOL, PETERSPLATZ 10, CH-4003 BASEL, SWITZERLAND (Reprint); UNIV BASEL, INST MED MIKROBIOL, CH-4003 BASEL, SWITZERLAND; UNIV LAUSANNE, FAC MED, INST BIOCHIM, CH-1066 EPALINGES, SWITZERLAND; OSAKA BIOSCI INST, DEPT BIOL MOLEC, OSAKA, JAPAN
COUNTRY OF AUTHOR: SWITZERLAND; JAPAN
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (SEP 1995) Vol. 25, No. 9, pp. 2679-2685. ISSN: 0014-2980.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 62
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Fas was recently demonstrated to be the major target molecule engaged by CD4(+) cytolytic T lymphocytes (CTL). We examined Fas expression on various cloned T cell subpopulations and their susceptibility to lysis by CD4(+) or CD8(+) CTL. A reciprocal relationship in Fas and Fas-ligand expression was observed in CD4(+) T helper (Th)1- and Th2-type clones, and Fas mRNA was predominantly detected in Th2 clones, whereas Fas-ligand mRNA was principally found in Th1 clones. The two Th0 clones tested expressed both Fas and Fas-ligand, but only one exhibited cytolytic activity, whereas both were sensitive to CD4-mediated lysis. A functional consequence of the inverse Fas-Fas-ligand expression pattern was that Th2 and Th0 cells were sensitive to lysis by both Th1 CD4(+) CTL and a CD8(+) CTL clone in a Fas-dependent manner. These results suggest that cytolytic CD4(+)

Th1 cells may play an immunomodulatory role, regulating a Th2/Th0 response by Fas-mediated lysis.

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E1 1 GORMAN DAN M/AU
E2 2 GORMAN DANIEL/AU
E3 18 --> GORMAN DANIEL M/AU
E4 1 GORMAN DANIEL PRESTON/AU
E5 3 GORMAN DANNIE J/AU
E6 5 GORMAN DAVID B/AU
E7 1 GORMAN DAVID BRUCE/AU
[redacted] 4 GORMAN DAVID J/AU
[redacted] 1 GORMAN DEAN/AU
E10 1 GORMAN DEBRA D/AU
E11 1 GORMAN DENNIE J/AU
E12 1 GORMAN DES/AU

=> s e3 or e2

L7 20 "GORMAN DANIEL M"/AU OR "GORMAN DANIEL"/AU

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L8 20 DUP REM L7 (0 DUPLICATES REMOVED)

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L8 ANSWER 1 OF 20 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1998:612170 CAPLUS
DOCUMENT NUMBER: 129:226639
TITLE: Cloning and cDNA sequences of human proteinase, oxidoreductase, and GTP-binding protein homologs
INVENTOR(S): Mueller, Christopher G.; Lebecque, Serge J. E.; Liu, Yong-jun; Dowling, Lynette M.; Huffine, Constance F.; **Gorman, Daniel M.**
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2

NUMBER	DATE
PATENT INFORMATION: WO 9839421 A2	19980911

DESIGNATED STATES: W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG

APPLICATION INFORMATION: WO 98-US3937 19980306
PRIORITY APPLN. INFO.: US 97-813150 19970307
DOCUMENT TYPE: Patent
LANGUAGE: English

AB Complementary DNA encoding various human proteins, reagents related thereto, including specific antibodies, and purified proteins are described. The BS10.55 gene was initially found by anal. of clones isolated from germinal center dendritic cells. The predicted amino acid sequences comprises 470 residues, including a signal peptide moiety, with the structural motifs of a member of the disintegrin-metalloproteinase family of proteases. The YTF03 gene was also detected in dendritic cells, codes for 567 amino acid residues including a signal peptide, and is similar to monoamine oxidase-like enzymes. The APD08 gene was detected in dendritic cells, codes for a GTP-binding protein/GTPase-like protein comprising 619 amino acid residues. Methods of using said reagents and related diagnostic kits are also provided.

L8 ANSWER 2 OF 20 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1998:527433 CAPLUS
DOCUMENT NUMBER: 129:157713
TITLE: Mammalian chemokines and transmembrane receptors and their uses
INVENTOR(S): Mattson, Jeanine D.; Soto-Trejo, Hortensia; Hedrick, Joseph A.; **Gorman, Daniel M.**; Zlotnik, Albert
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2

NUMBER	DATE
PATENT INFORMATION: WO 9832858 A2	19980730

DESIGNATED STATES: W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG

APPLICATION INFORMATION: WO 98-US902 19980122
PRIORITY APPLN. INFO.: US 97-36715 19970123
DOCUMENT TYPE: Patent
LANGUAGE: English

AB Claimes include novel chemokines and 7 transmembrane receptors from mammals, reagents related thereto, including purified proteins, specific antibodies, and nucleic acids encoding said chemokines or receptors. Methods of using said reagents and diagnostic kits are also provided. The chemokines and chemokine receptors include proteins CXC-143, IBICK, MCP243, R277, HST01.1, and 942D12. The cDNA sequences and encoded amino acid sequences are presented.

L8 ANSWER 3 OF 20 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1998:509290 CAPLUS
DOCUMENT NUMBER: 129:160633
TITLE: Mammalian chemokines; receptors; reagents; uses
INVENTOR(S): Huffine, Constance F.; Rossi, Devora L.; Capone, Myriam; Hedrick, Joseph A.; Vicari, Alain; **Gorman, Daniel M.**; Zlotnik, Albert
PATENT ASSIGNEE(S): Schering Corp., USA
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2

NUMBER	DATE
PATENT INFORMATION: WO 9831810 A2	19980723

DESIGNATED STATES: W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA,

UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG

APPLICATION INFORMATION: WO 98-US218 19980120
PRIORITY APPLN. INFO.: US 97-786624 19970121
DOCUMENT TYPE: Patent
LANGUAGE: English

AB Chemokines and 7 transmembrane receptors from mammals, reagents related thereto, including purified proteins, specific antibodies, and nucleic acids encoding said chemokines or receptors. Methods of using said reagents and diagnostic kits are also provided. The invention further provides methods of modulating physiol. or development of a cell, such as neuron, macrophage or lymphocyte, by contacting the cell with a compn. comprising an agonist or antagonist or the receptor. The physiol. effects to be modulated include a cellular calcium flux, a chemoattractant response, cellular morphol. modification responses, phosphoinositide lipid turnover, or an antiviral response.

L8 ANSWER 4 OF 20 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1998:424268 CAPLUS
DOCUMENT NUMBER: 129:94454
TITLE: Mammalian cell surface antigens 63954 and antibodies and genes
INVENTOR(S): Gorman, Daniel M.
PATENT ASSIGNEE(S): Schering Corp., USA
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2

	NUMBER	DATE
PATENT INFORMATION:	WO 9827114 A2	19980625
DESIGNATED STATES:	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG		

APPLICATION INFORMATION: WO 97-US23321 19971216
PRIORITY APPLN. INFO.: US 96-33601 19961217
DOCUMENT TYPE: Patent
LANGUAGE: English

AB Purified genes encoding a T cell surface antigen from a mammal, designated 63954, reagents related thereto including purified proteins, specific antibodies, and nucleic acids encoding this antigen are provided. The antigen acts as inducer of apoptosis and modulates antigen-specific proliferation and cytokine prodn. by effector cells. Methods of using said reagents and diagnostic kits are also provided.

L8 ANSWER 5 OF 20 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1998:405980 CAPLUS
DOCUMENT NUMBER: 129:80627
TITLE: T cell surface antigen 499E9 of mouse, cDNA encoding 499E9, and production of 499E9 with recombinant cells
INVENTOR(S): Gorman, Daniel M.; Mattson, Jeanine D.
PATENT ASSIGNEE(S): Schering Corp., USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2

	NUMBER	DATE
PATENT INFORMATION:	WO 9825958 A2	19980618
DESIGNATED STATES:	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG		

APPLICATION INFORMATION: WO 97-US22766 19971212
PRIORITY APPLN. INFO.: US 96-32846 19961213
DOCUMENT TYPE: Patent
LANGUAGE: English

AB CDNA encoding a T cell surface antigen from mouse, reagents related thereto including purified proteins, specific antibodies, and nucleic acids encoding this antigen are provided. Methods of using said reagents and diagnostic kits are also provided. The cDNA for protein 499E9, which is expressed on the surface of highly polarized mouse Th1 T cells, was cloned and sequenced. The 316-amino acid protein is a type II transmembrane protein which exhibits structural motifs characteristic of a member of the TNF ligand family. Transcript anal. identified multiple transcripts with the most prevalent being 2.1-2.3 kb. Southern anal. indicated 499E9 is produced in many T cells although pos. signals were also found in brain, heart, kidney, liver, lung, spleen and testis.

L8 ANSWER 6 OF 20 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1998:398416 CAPLUS
DOCUMENT NUMBER: 129:77573
TITLE: Human monocyte-specific genes and gene products and their uses
INVENTOR(S): Adema, Gosse Jan; Meyaard, Linde; Gorman, Daniel M.; McClanahan, Terrill K.; Zurawski, Sandra M.; Zurawski, Gerard; Lanier, Lewis L.; Phillips, Joseph H.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2

	NUMBER	DATE
PATENT INFORMATION:	WO 9824906 A2	19980611
DESIGNATED STATES:	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG		

APPLICATION INFORMATION: WO 97-US21101 19971205
PRIORITY APPLN. INFO.: US 96-32252 19961206
US 96-762187 19961209
US 96-33181 19961216
US 97-41279 19970321
DOCUMENT TYPE: Patent
LANGUAGE: English

AB A group of cDNAs expressed specifically in human monocytes are identified and cloned. The proteins encoded by these cDNAs have Ig-like structural features or are Ig receptor-like. One of the

proteins, an Ig receptor homolog, appears to play a role in cell killing by NK cells.

L8 ANSWER 7 OF 20 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1998:184018 CAPLUS
DOCUMENT NUMBER: 128:256391
TITLE: Mammalian C-C and C-X-C chemokines, and their cDNA sequences and diagnostic and therapeutic uses
INVENTOR(S): Gorman, Daniel M.; Hedrick, Joseph A.; Zlotnik, Albert
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2

	NUMBER	DATE
PATENT INFORMATION:	WO 9811226 A2	19980319

DESIGNATED STATES: W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
APPLICATION INFORMATION: WO 97-US15315 19970909
PRIORITY APPLN. INFO.: US 96-25724 19960910
DOCUMENT TYPE: Patent
LANGUAGE: English
AB Novel CC and CXC chemokines from humans, reagents related thereto including purified proteins, specific antibodies, and nucleic acids encoding these chemokines are provided. Two chemokine-motif-contg. mols. designated 61164 and 331D5 are classified as belonging to the C-X-C chemokine family and C-C chemokine family, resp., based on sequence anal. The tissue distribution of 61164 suggests that it may be produced by B cells, whereas 331D5 is assocd. with T cells. The cDNA and deduced amino acid sequence of human and murine 61164 and 331D5 are provided. Also provided are methods of making and using said reagents and diagnostic kits.

L8 ANSWER 8 OF 20 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1998:126352 CAPLUS
DOCUMENT NUMBER: 128:204066
TITLE: Mammalian T cell surface antigen 312C2 and its cDNA sequence and therapeutic applications
INVENTOR(S): Gorman, Daniel M.; Randall, Troy D.; Zlotnik, Albert
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2

	NUMBER	DATE
PATENT INFORMATION:	WO 9806842 A1	19980219

DESIGNATED STATES: W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
APPLICATION INFORMATION: WO 97-US13931 19970814
PRIORITY APPLN. INFO.: US 96-689943 19960816
US 96-27901 19961007
DOCUMENT TYPE: Patent
LANGUAGE: English
AB Purified genes encoding murine and human cell surface antigens (designated m312C2 and h312C2), reagents related thereto including purified proteins, specific antibodies, and nucleic acids encoding these antigens are provided. These genes are expressed in the thymus, and are induced on T cells and spleen cells following activation. Engagement of 312C2 stimulates proliferation of T cell clones, antigen-specific proliferation, and cytokine prodn. by T cells, and appears to potentiate T cell expansion or apoptosis. Northern anal. shows that 312C2 is expressed in various Th1, Th2, CD4+, CD8+, NK1.1+, pro-, pre-, .alpha..beta.CD4-CD8- T cells, thymus, and activated spleen cells, but is virtually absent in lung, heart, kidney, macrophage, stroma, brain, liver, muscle, and testes. With human 312C2, 6 alternatively processed forms have been isolated. Methods of using said reagents and diagnostic kits are also provided.

L8 ANSWER 9 OF 20 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1998:425101 CAPLUS
DOCUMENT NUMBER: 129:199681
TITLE: Leukocystatin, a new class II cystatin expressed selectively by hematopoietic cells
AUTHOR(S): Halfon, Sherin; Ford, John; Foster, Jessica; Dowling, Lynette; Lucian, Linda; Sterling, Marissa; Xu, Yuming; Weiss, Mary; Ikeda, Mami; Liggett, Debra; Helms, Allison; Caux, Christopher; Lebecque, Serge; Hannum, Chuck; Menon, Satish; McClanahan, Terrill; Gorman, Daniel; Zurawski, Gerard
CORPORATE SOURCE: Dep. Mol. Biol., DNAX Res. Inst., Palo Alto, CA, 94304-1104, USA
SOURCE: J. Biol. Chem. (1998), 273(26), 16400-16408
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors describe a new cystatin in both mice and humans, which the authors termed leukocystatin. This protein has all the features of a Class II secreted inhibitory cystatin but contains lysine residues in the normally hydrophobic binding regions. As detd. by cDNA library Southern blots, this cystatin is expressed selectively in hematopoietic cells, although fine details of the distribution among these cell types differ between the human and mouse mRNAs. In addn., the authors have detd. the genomic organization of mouse leukocystatin, and the authors found that in contrast to most cystatins, the leukocystatin gene contains three introns. The recombinant proteins corresponding to these cystatins were expressed in Escherichia coli as N-terminal glutathione S-transferase or FLAG fusions, and studies showed that they inhibited papain and cathepsin L but with affinities lower than other cystatins. The unique features of leukocystatin suggests that this cystatin plays a role in immune regulation through inhibition of a unique target in the hematopoietic system.

L8 ANSWER 10 OF 20 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1998:421010 CAPLUS
DOCUMENT NUMBER: 129:159993
TITLE: Identification and characterization of a constitutively active STAT5 mutant that promotes

cell proliferation

AUTHOR(S): Onishi, Mayumi; Nosaka, Tetsuya; Misawa, Kazuhide; Mui, Alice L. -F.; Gorman, Daniel; Mcmahon, Martin; Miyajima, Atsushi; Kitamura, Toshio

CORPORATE SOURCE: Department of Cell Signaling, DNAX Research Institute of Molecular and Cell Biology, Palo Alto, CA, 94304, USA

SOURCE: Mol. Cell. Biol. (1998), 18(7), 3871-3879
CODEN: MCEBD4; ISSN: 0270-7306

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB STAT (signal transducers and activators of transcription) proteins are transcription factors which are activated by phosphorylation on tyrosine residues upon stimulation by cytokines. Seven members of the STAT family are known, including the closely related STAT5A and STAT5B, which are activated by various cytokines. Except for prolactin-dependent .beta.-casein prodn. in mammary gland cells, the biol. consequences of STAT5 activation in various systems are not clear. The authors applied PCR-driven random mutagenesis and a retrovirus-mediated expression screening system to identify constitutively active forms of STAT5. By this strategy, the authors have identified a constitutively active STAT5 mutant which has two amino acid substitutions; one is located upstream of the putative DNA binding domain (H299R), and the other is located in the transactivation domain (S711F). The mutant STAT5 was constitutively phosphorylated on tyrosine residues, localized in the nucleus, and was transcriptionally active. Expression of the mutant STAT5 partially dispenses with interleukin 3 (IL-3) as a growth stimulant of IL-3-dependent cell lines. Further analyses of the mutant STAT5 have demonstrated that both of the mutations are required for nuclear localization, efficient transcriptional activation, and induction of IL-3-independent growth of an IL-3-dependent cell line, Ba/F3, and have indicated that a mol. basis for the constitutive activation is the stability of the phosphorylated form of the mutant STAT5.

L8 ANSWER 11 OF 20 CAPLUS COPYRIGHT 1998 ACS

ACCESSION NUMBER: 1997:440457 CAPLUS

DOCUMENT NUMBER: 127:218269

TITLE: HNMP-1: a novel hematopoietic and neural membrane protein differentially regulated in neural development and injury

AUTHOR(S): Bolin, Laurel M.; McNeil, Tom; Lucian, Linda A.; DeVaux, Brigitte; Franz-Bacon, Karin; Gorman, Daniel M.; Zurawski, Sandra; Murray, Richard; McClanahan, Terrill K.

CORPORATE SOURCE: DNAX Research Institute, Palo Alto, CA, 94304-1104, USA

SOURCE: J. Neurosci. (1997), 17(14), 5493-5502
CODEN: JNRSDS; ISSN: 0270-6474

PUBLISHER: Society for Neuroscience

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The hnmp-1 (hematopoietic neural membrane protein) gene encodes a protein with striking similarity to the tetra-transmembrane-spanning protein encoded by pmp22. Hnmp-1 was cloned from an elutriated human monocyte library and is expressed in various human hematopoietic and lymphoid lineages as well as adult mouse spleen and thymus. In the mouse nervous system, HNMP-1 mRNA is temporally expressed by Schwann cells during sciatic nerve myelination. Dorsal root ganglia sensory and spinal cord .alpha.-motoneurons acquire HNMP-1 protein selectively throughout development. In the fiber tracts of the spinal cord and in sciatic nerve, HNMP-1 protein is axon-assocd. Addnl. a rapid and sustained level of HNMP-1 expression is obsd. in response to acute PNS injury. HNMP-1 is constitutively induced in sciatic nerve of Trembler J mice, which are mutant for pmp22 and have a demyelinating/hypomyelinating phenotype. The expression pattern of HNMP-1 suggests a possible role for this mol. during active myelination.

L8 ANSWER 12 OF 20 CAPLUS COPYRIGHT 1998 ACS

ACCESSION NUMBER: 1996:456134 CAPLUS

DOCUMENT NUMBER: 125:139968

TITLE: Identification through bioinformatics of cDNAs encoding human thymic shared Ag-1/stem cell Ag-2. A new member of the human Ly-6 family

AUTHOR(S): Capone, Myriam C.; Gorman, Daniel M.; Ching, Edwin P.; Zlotnik, Albert

CORPORATE SOURCE: DNAX Res. Inst. Molecular Cellular Biology, Palo Alto, CA, USA

SOURCE: J. Immmnol. (1996), 157(3), 969-973
CODEN: JOIMA3; ISSN: 0022-1767

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The Ly-6 family of cell surface mols. includes many members that have been characterized in the mouse. Until recently, very few Ly-6 family members had been described in the human. A significant development with important implications for novel gene discovery has been the growth of the public Expressed Sequence Tag (EST) database. Here the authors report that, through the application of bioinformatics anal. to the dbEST database, the authors obtained the sequence of human TSA-1/SCA-2, a new member of the human Ly-6 family. In addn., the authors identified full-length clones encoding this mol. as well as expression data in various tissues. Sequencing of the clones identified in this way confirmed the sequence predicted through bioinformatics. This study constitutes an example of the application of bioinformatics to the anal. of the recently expanded databases for the identification of genes of potential importance in the immune system.

L8 ANSWER 13 OF 20 CAPLUS COPYRIGHT 1998 ACS

ACCESSION NUMBER: 1995:462926 CAPLUS

DOCUMENT NUMBER: 122:237468

TITLE: Impaired interleukin-3 (IL-3) response of the A/J mouse is caused by a branch point deletion in the IL-3 receptor .alpha. subunit gene

AUTHOR(S): Ichihara, Masatoshi; Hara, Takahiko; Takagi, Mineo; Cho, Lori C.; Gorman, Daniel M.; Miyajima, Atsushi

CORPORATE SOURCE: Dep. Cell Biology, DNAX Research Inst. Molecular Cellular Biology, Palo Alto, CA, 94304, USA

SOURCE: EMBO J. (1995), 14(5), 939-50
CODEN: EMJODG; ISSN: 0261-4189

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Interleukin-3 (IL-3) alone does not support hematopoietic colony formation of bone marrow cells from the A/J mouse. To elucidate the mol. lesion in A/J mice, the authors examd. expression of the .alpha. and .beta. subunits of the IL-3 receptor (IL-3R). While IL-3R.beta. was normally expressed, IL-3R.alpha. was not detectable on the surface of A/J-derived cells by antibody staining. Genetic linkage anal. using recombinant inbred mouse strains between A/J and IL-3-responsive C57BL/6 indicated that the IL-3R.alpha. gene locus was responsible for the impaired IL-3 response in A/J mice. Mol. cloning and characterization of A/J-derived IL-3R.alpha. cDNA revealed that it lacked the sequence corresponding to exon 8, which encodes 10 amino acid residues in the extracellular domain. The

aberrant splicing was due to a 5 base pair deletion at the branch point in intron 7 and was reproduced in heterologous cells by transfecting within an IL-3R.alpha. minigene carrying the deleterious intron. The A/J-specific abnormal form of IL-3R.alpha. was localized inside the cells, but not on the cell surface, providing the mol. basis for the impaired IL-3 response in the A/J mouse.

L8 ANSWER 14 OF 20 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1995:92226 CAPLUS
DOCUMENT NUMBER: 122:78793
TITLE: Subset of CD4+ T cell clones expressing IL-3 receptor .alpha.-chains uses IL-3 as a cofactor in autocrine growth
AUTHOR(S): Mueller, Daniel L.; Chen, Zong-Ming; Schwartz, Ronald H.; **Gorman, Daniel M.**; Kennedy, Mary K.
CORPORATE SOURCE: Med. Sch., Univ. Minnesota, Minneapolis, MN, 55455, USA
SOURCE: J. Immunol. (1994), 153(7), 3014-27
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In this paper the authors demonstrate that IL-3 can act as a cofactor for the growth of some CD4+ T cells. This lymphokine synergized with IL-4 to induce both a unique set of protein tyrosine phosphorylations and the vigorous proliferation of the keyhole limpet hemocyanin-specific and I-Ab-restricted CD4+ Th0 cell clone, E6. In addn., neutralizing anti-IL-3 Abs specifically inhibited the growth of E6 T cells to Ag or anti-CD3 mAb stimulation. Finally, this T cell clone was shown to express both the IL-3R .alpha.-chain and an IL-3R .beta.-chain (AIC2A). An examn. of other CD4+ T cell clones detd. that one Th1 clone (A.E7), two Th0 clones (16B.2 and L9A.1), and one Th2 clone (D10.G4.1) were not influenced by the addn. of rIL-3. However, proliferation of the Th2 clones CDC25 and CDC35 to CD3-stimulation was significantly enhanced by IL-3. The sensitivity of these latter two clones to IL-3 was also found to be assocd. with expression of IL-3R .alpha.-chains. Because E6 T cells are highly dependent on IL-4 for autocrine growth similar to Th2 cells, these results suggest that IL-3 may synergize with IL-4 to enhance the proliferation of a subset of IL-4-dependent CD4+ T cells, and the study indicates that IL-3R .alpha.-chain expression may be a specific marker of this CD4+ T cell subset.

L8 ANSWER 15 OF 20 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1993:248796 CAPLUS
DOCUMENT NUMBER: 118:248796
TITLE: Chromosomal localization and organization of the murine genes encoding the .beta. subunits (AIC2A and AIC2B) of the interleukin 3, granulocyte/macrophage colony-stimulating factor, and interleukin 5 receptors
AUTHOR(S): **Gorman, Daniel M.**; Itoh, Naoto; Jenkins, Nancy A.; Gilbert, Debra J.; Copeland, Neal G.; Miyajima, Atsushi
CORPORATE SOURCE: Dep. Mol. Biol., DNAX Res. Inst. Mol. Cell. Biol., Palo Alto, CA, 94304, USA
SOURCE: J. Biol. Chem. (1992), 267(22), 15842-8
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Chromosomal genes for two mouse homologous .beta. subunits (AIC2A and AIC2B) of the interleukin-3, granulocyte/macrophage colony-stimulating factor, and interleukin-5 receptors were characterized. Both AIC2A and AIC2B genes were present on a 250-kilobase MluI restriction fragment and were mapped on murine chromosome 15 (these loci were provisionally designated as Il3rb-1 (AIC2A) and Il3rb-2 (AIC2B), closely linked to the c-sis locus. Both genes consist of 14 exons and span about 28 kb each. The major transcription initiation sites of both genes were mapped at 194 bp from the initiation codon. These genes are 95% identical up to 700 bp from the transcription initiation sites. Potential recognition sequences for hemopoietic transcription factors including GATA-1 and PU.1 in addn. to a TATA-like sequence are present in the 5'-flanking region. A stretch of 20 bp including the initiation site is homologous to the corresponding region of the erythropoietin receptor and the interleukin-7 receptor genes and to the initiator sequence of the adeno-assocd. virus P5 promoter, suggesting a possible role in transcription initiation. Comparison of the exon/intron boundaries of AIC2A and AIC2B genes with those of other members of the cytokine receptor superfamily reveals a conserved evolutionary structure. Isolation of various forms of AIC2 cDNAs reveals differential splicing of the transcripts.

L8 ANSWER 16 OF 20 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1993:426077 CAPLUS
DOCUMENT NUMBER: 119:26077
TITLE: Cytokine receptors: A new superfamily of receptors
AUTHOR(S): Schreurs, Jolanda; **Gorman, Daniel M.**; Miyajima, Atsushi
CORPORATE SOURCE: Dep. Protein Chem., Chiron Corp., Emeryville, CA, 94608, USA
SOURCE: Int. Rev. Cytol. (1992), 137B(Molecular Biology of Receptors and Transporters), 121-55
CODEN: IRCYAJ; ISSN: 0074-7696
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 192 refs., providing a summary of the following: (1) the characteristics that define the structure and compn. of the receptors and their ability to bind ligand and transduce signals, (2) known signal transduction pathways, and (3) the evidence for oncogenic processes dependent on aberrant cytokine receptor interactions.

L8 ANSWER 17 OF 20 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1991:442975 CAPLUS
DOCUMENT NUMBER: 115:42975
TITLE: Molecular cloning of a second subunit of the receptor for human granulocyte-macrophage colony-stimulating factor (GM-CSF): reconstitution of a high-affinity GM-CSF receptor
AUTHOR(S): Hayashida, Kazuhiro; Kitamura, Toshio; **Gorman, Daniel M.**; Arai, Kenichi; Yokota, Takashi; Miyajima, Atsushi
CORPORATE SOURCE: Res. Inst. Mol. Cell. Biol., DNAX, Palo Alto, CA, 94304, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1990), 87(24), 9655-9
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Using the mouse interleukin 3 (IL-3) receptor cDNA as a probe, a homologous cDNA (KH97) was obtained from a cDNA library of a human hemopoietic cell line, TF-1. The protein encoded by the KH97 cDNA has 56% amino acid sequence identity with the mouse IL-3 receptor and retains features common to the family of cytokine receptors. Fibroblasts transfected with the KH97 cDNA expressed a protein of

120 kDa but did not bind any human cytokines, including IL-3 and granulocyte-macrophage colony-stimulating factor (GM-CSF). Interestingly, cotransfection of cDNAs for KH97 and the low-affinity human GM-CSF receptor in fibroblasts resulted in formation of a high-affinity receptor for GM-CSF. The dissocn. rate of GM-CSF from the reconstituted high-affinity receptor was slower than that from the low-affinity site, whereas the assocn. rate was unchanged. Crosslinking of 125I-labeled GM-CSF to fibroblasts cotransfected with both cDNAs revealed the same crosslinking patterns as in TF-1 cells-i.e., 2 major proteins of 80 and 120 kDa which correspond to the low-affinity GM-CSF receptor and the KH97 protein, resp. These results indicate that the high-affinity GM-CSF receptor is composed of at least 2 components in a manner analogous to the IL-2 receptor. It was therefore proposed to designate the low-affinity GM-CSF receptor and the KH97 protein as the .alpha. and .beta. subunits of the GM-CSF receptor, resp.

L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1990:605819 CAPLUS
DOCUMENT NUMBER: 113:205819
TITLE: Cloning and expression of a gene encoding an interleukin 3 receptor-like protein: identification of another member of the cytokine receptor gene family
AUTHOR(S): **Gorman, Daniel M.**; Itoh, Naoto; Kitamura, Toshio; Schreurs, Jolanda; Yonehara, Shin; Yahara, Ichiro; Arai, Kenichi; Miyajima, Atsushi
CORPORATE SOURCE: DNAX Res. Inst. Mol. Cellular Biol., Palo Alto, CA, 94304, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1990), 87(14), 5459-63
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Using a monoclonal antibody to the interleukin 3 (IL-3) receptor (anti-Aic2), a cDNA (AIC2B) was isolated from a mouse mast cell line which is homologous to the previously characterized gene for the IL-3 receptor (AIC2A). This cDNA encodes a polypeptide of 896 amino acid residues and has 91 % amino acid sequence identity with the IL-3 receptor. A consensus sequence defining an addnl. cytokine receptor family is present in this clone. Compared to the AIC2A clone, the AIC2B cDNA encodes a protein with amino acid substitutions, insertions, and deletions dispersed throughout the entire protein. Oligonucleotide probes specific for each cDNA hybridized with different genomic fragments, indicating that the AIC2A and AIC2B proteins are encoded by 2 distinct genes. Fibroblasts transfected with the AIC2B cDNA expressed the protein at the cell surface, as detd. by binding with the anti-Aic2 antibody, but did not bind IL-3 or other cytokines, including IL-2, IL-4, granulocyte-macrophage colony-stimulating factor, erythropoietin, and IL-9 (p40) at concns. between 1 and 10 nM. An S1 nuclease assay was used to discriminate between the AIC2A and AIC2B transcripts. The AIC2B gene was coexpressed with the AIC2A gene. These results suggest a potential involvement of AIC2B in cytokine signal transduction.

L8 ANSWER 19 OF 20 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1990:492267 CAPLUS
DOCUMENT NUMBER: 113:92267
TITLE: Expression cloning of a cDNA encoding the murine interleukin 4 receptor based on ligand binding
AUTHOR(S): Harada, Nobuyuki; Castle, Brian E.; **Gorman, Daniel M.**; Itoh, Naoto; Schreurs, Jolanda; Barrett, Robin L.; Howard, Maureen; Miyajima, Atsushi
CORPORATE SOURCE: Dep. Immunol., DNAX Res. Inst. Mol. Cell. Biol., Palo Alto, CA, 94304, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1990), 87(3), 857-61
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Interleukin 4 (IL-4) is a potent mediator of growth and differentiation for various lymphoid and myeloid cells. To isolate a cDNA encoding the murine IL-4 receptor, an expression cloning method was developed that uses biotinylated ligand as a probe and that may be generally applicable to cloning of receptor genes. COS-7 cells transiently transfected with the cloned full-length cDNA bind murine IL-4 specifically with a Kd = 165 pM. Crosslinking of 125I-labeled IL-4 to COS-7 cells transfected with the cDNA reveals binding to proteins of 120-140 kDa. IL-4-responsive cells also express IL-4-binding proteins of 120-140 kDa but show addnl. bands at 60-70 kDa; the relationship of the smaller proteins to the larger ones is unclear. The nucleotide sequence indicates that the full-length cDNA encodes 810 amino acids including the signal sequence. While no consensus sequence for protein kinases is present in the cytoplasmic domain, a sequence comparison with the erythropoietin receptor, the IL-6 receptor, and the .beta. chain of the IL-2 receptor reveals a significant homol. in the extracellular domain, indicating that the IL-4 receptor is a member of a cytokine receptor family.

L8 ANSWER 20 OF 20 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1990:152976 CAPLUS
DOCUMENT NUMBER: 112:152976
TITLE: Cloning of an interleukin-3 receptor gene: a member of a distinct receptor gene family
AUTHOR(S): Itoh, Naoto; Yonehara, Shin; Schreurs, Jolanda; **Gorman, Daniel M.**; Maruyama, Kazuo; Ishii, Ai; Yahara, Ichiro; Arai, Kenichi; Miyajima, Atsushi
CORPORATE SOURCE: Dep. Mol. Biol., DNAX Res. Inst. Mol. Cell. Biol., Palo Alto, CA, 94304, USA
SOURCE: Science (Washington, D. C., 1883-) (1990), 247(4940), 324-7
CODEN: SCIEAS; ISSN: 0036-8075
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Interleukin-3 (IL-3) binds to its receptor with high and low affinities, induces tyrosine phosphorylation, and promotes the proliferation and differentiation of hematopoietic cells. A binding component of the IL-3 receptor was cloned. Fibroblasts transfected with the cDNA bound IL-3 with a low affinity [dissocn. const. (Kd) of 17.9 nM]. No consensus sequence for a tyrosine kinase was present in the cytoplasmic domain. Thus, addnl. components are required for a functional high affinity IL-3 receptor. A sequence comparison of the IL-3 receptor with other cytokine receptors (erythropoietin, IL-4, IL-6, and the .beta. chain IL-2 receptor) revealed a common motif of a distinct receptor gene family.

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E2	3	MATTSON JEANINE/AU
E3	3 -->	MATTSON JEANINE D/AU
E4	1	MATTSON JENS G/AU
E5	1	MATTSON JIM/AU
E6	8	MATTSON JOAN C/AU
E7	1	MATTSON JOANNE M/AU

E8 1 MATTSON JOEL L/AU

E9 1 MATTSON JOHN EDWARD/AU

E10 4 MATTSON JOHN P/AU

E11 1 MATTSON JOHN PAUL/AU

E12 3 MATTSON JOHN R/AU

=> s e2 or e3

L9 6 "MATTSON JEANINE"/AU OR "MATTSON JEANINE D"/AU

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L10 ANSWER 1 OF 6 CAPLUS COPYRIGHT 1998 ACS

ACCESSION NUMBER: 1998:527433 CAPLUS

DOCUMENT NUMBER: 129:157713

TITLE: Mammalian chemokines and transmembrane receptors and their uses

INVENTOR(S): **Mattson, Jeanine D.**; Soto-Trejo, Hortensia; Hedrick, Joseph A.; Gorman, Daniel M.; Zlotnik, Albert

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2

	NUMBER	DATE
PATENT INFORMATION:	WO 9832858 A2	19980730

DESIGNATED STATES: W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG

APPLICATION INFORMATION: WO 98-US902 19980122

PRIORITY APPLN. INFO.: US 97-36715 19970123

DOCUMENT TYPE: Patent

LANGUAGE: English

AB Claimes include novel chemokines and 7 transmembrane receptors from mammals, reagents related thereto, including purified proteins, specific antibodies, and nucleic acids encoding said chemokines or receptors. Methods of using said reagents and diagnostic kits are also provided. The chemokines and chemokine receptors include proteins CXC-143, IBICK, MCP243, R277, HST01.1, and 942D12. The cDNA sequences and encoded amino acid sequences are presented.

L10 ANSWER 2 OF 6 CAPLUS COPYRIGHT 1998 ACS

ACCESSION NUMBER: 1998:405980 CAPLUS

DOCUMENT NUMBER: 129:80627

TITLE: T cell surface antigen 499E9 of mouse, cDNA encoding 499E9, and production of 499E9 with recombinant cells

INVENTOR(S): Gorman, Daniel M.; **Mattson, Jeanine D.**

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2

	NUMBER	DATE
PATENT INFORMATION:	WO 9825958 A2	19980618

DESIGNATED STATES: W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG

APPLICATION INFORMATION: WO 97-US22766 19971212

PRIORITY APPLN. INFO.: US 96-32846 19961213

DOCUMENT TYPE: Patent

LANGUAGE: English

AB CDNA encoding a T cell surface antigen from mouse, reagents related thereto including purified proteins, specific antibodies, and nucleic acids encoding this antigen are provided. Methods of using said reagents and diagnostic kits are also provided. The cDNA for protein 499E9, which is expressed on the surface of highly polarized mouse Th1 T cells, was cloned and sequenced. The 316-amino acid protein is a type II transmembrane protein which exhibits structural motifs characteristic of a member of the TNF ligand family. Transcript anal. identified multiple transcripts with the most prevalent being 2.1-2.3 kb. Southern anal. indicated 499E9 is produced in many T cells although pos. signals were also found in brain, heart, kidney, liver, lung, spleen and testis.

L10 ANSWER 3 OF 6 CAPLUS COPYRIGHT 1998 ACS

ACCESSION NUMBER: 1996:656802 CAPLUS

DOCUMENT NUMBER: 126:2018

TITLE: Biochemical and genetic characterization of multiple splice variants of the Flt3 ligand

AUTHOR(S): McClanahan, Terrill; Culpepper, Janice; Campbell, David; Wagner, Janet; Franz-Bacon, Karin; **Mattson, Jeanine**; Tsai, Shirley; Luh, Jeanne; Guimaraes, M. Jorge; et al.

CORPORATE SOURCE: Dep. Mol. Biol., DNAX Res. Inst. Mol. Cell. Biol., Palo Alto, CA, 94304, USA

SOURCE: Blood (1996), 88(9), 3371-3382
CODEN: BLOOAW; ISSN: 0006-4971

PUBLISHER: Saunders

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A comprehensive anal. of cell lines and tissues was performed to compare and contrast the expression patterns of Flt3 ligand (FL), c-Kit ligand (KL), and macrophage colony-stimulating factor as well as their receptors, Flt3, c-Kit, and c-Fms. The message for FL is unusually ubiquitous, whereas that of its receptor is quite restricted, apparently limiting the function of the ligand to fetal development and early hematopoiesis. Also, a mouse FL genomic clone was sequenced, revealing how the 3 splice variant FL mRNAs that have been isolated arise. The chromosomal location of the FL gene was mapped, by in situ hybridization, to chromosome 7 in mouse and chromosome 19 in human. Natural FL protein was purified from a stromal cell line and shown to be a 65-kDa nondisulfide-linked homodimeric glycoprotein comprised of 30-kDa subunits, each contg. 12 kDa of N- and O-linked sugars. Pulse-chase expts. show that one of the splice variants (T110) is responsible for producing the bulk of sol. FL, but only after it has first been expressed at the cell

surface as a membrane-bound form. The other splice-variant forms produce mols. that are either obligatorily sol. (T169) or membrane-bound but released only very slowly (T118). Finally, even though most cell lines express some amt. of FL mRNA, very little FL protein is actually made, with T cells and stromal cells being the major producers. The data suggests that FL plays its roles over very short distances, perhaps requiring cell-cell contact.

L10 ANSWER 4 OF 6 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1996:408726 CAPLUS
DOCUMENT NUMBER: 125:135153
TITLE: Molecular cloning and sequencing of cDNAs encoding insecticidal peptides from the primitive hunting spider, Plectreurys tristis (Simon)
AUTHOR(S): Leisy, Douglas J.; Mattson, Jeanine D.; Quistad, Gary B.; Kramer, Steven J.; Van Beek, Nikolai; Tsai, Leslie W.; Enderlin, Frances E.; Woodworth, Alison R.; Digan, Mary Ellen
CORPORATE SOURCE: Sandoz Agro Inc., Palo Alto, CA, 94304, USA
SOURCE: Insect Biochem. Mol. Biol. (1996), 26(5), 411-417
CODEN: IBMBES; ISSN: 0965-1748
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Plectreurys tristis cephalothorax mRNA was isolated and amplified by PCR using degenerate primers corresponding to reverse translated mature Plt-VI toxin. An oligonucleotide corresponding to a portion of the amplified product was then used to screen a P. tristis cDNA library. The cDNAs from 10 pos. clones were sequenced. Eight of these cDNAs corresponded to Plt-VI toxin, one to Plt-XI toxin, and one was very similar to Plt-VIII toxin, with the exception of a single amino acid substitution. Anal. of these cDNAs indicated that these toxins are initially synthesized as prepro-forms which undergo signal cleavage followed by addnl. processing at both their N- and C-termini to produce the mature products.

L10 ANSWER 5 OF 6 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1996:536035 CAPLUS
DOCUMENT NUMBER: 125:192939
TITLE: CD94 and a novel associated protein (94AP) form a NK cell receptor involved in the recognition of HLA-A, HLA-B, and HLA-C allotypes
AUTHOR(S): Phillips, Joseph H.; Chang, Chiwen; Mattson, Jeanine; Gumperz, Jenny E.; Parham, Peter; Lanier, Lewis L.
CORPORATE SOURCE: Dep. Human Immunology Mol. Biology, DNAX Res. Inst. Mol. Cellular Biology, Palo Alto, CA, 94304, USA
SOURCE: Immunity (1996), 5(2), 163-172
CODEN: IUNIEH; ISSN: 1074-7613
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Whereas the human killer cell inhibitory receptors (KIRs) for HLA class I are Ig-like monomeric type I glycoproteins, the murine Ly49 receptors for H-2 are type II homodimers of the C-type lectin superfamily. Here, we demonstrate that human NK cells also express C-type lectin receptors that influence recognition of polymorphic HLA-A, HLA-B, and HLA-C mols. These receptors are heterodimers composed of CD94 chains covalently assocd. with novel tyrosine-phosphorylated glycoproteins (94AP). Some NK clones recognize a common HLA-C ligand using both KIRs and CD94-94AP receptors. These findings suggest the existence of human inhibitory MHC class I receptors of the Ig and C-type lectin superfamilies and indicate overlap in ligand specificity.

L10 ANSWER 6 OF 6 CAPLUS COPYRIGHT 1998 ACS
ACCESSION NUMBER: 1994:455833 CAPLUS
DOCUMENT NUMBER: 121:55833
TITLE: B7 and interleukin 12 cooperate for proliferation and interferon .gamma. production by mouse T helper clones that are unresponsive to B7 costimulation
AUTHOR(S): Murphy, Erin E.; Terres, Geronimo; Macatonia, Steven E.; Hsieh, Chyi Song; Mattson, Jeanine; Lanier, Lewis; Wysocka, Maria; Trinchieri, Giorgio; Murphy, Kenneth; O'Garra, Anne
CORPORATE SOURCE: DNAX Res. Inst., Palo Alto, CA, 94304-1104, USA
SOURCE: J. Exp. Med. (1994), 180(1), 223-32
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It was previously shown that dendritic cells isolated after overnight culture, which can express B7 and are potent stimulators of naive T cell proliferation, are relatively poor at inducing the proliferation of a panel of murine T helper 1 (Th1) clones. Maximal stimulation of Th1 clones was achieved using unsepd. splenic antigen presenting cells (APC). Here it was shown that FcR+ L cells transfected with B7 stimulate minimal proliferation of Th1 clones in response to anti-CD3 antibodies, in contrast to induction of significant proliferation of naive T cells. However, addn. of interleukin 12 (IL-12) to cultures of Th1 cells stimulated with anti-CD3 and FcR+ B7 transfectants resulted in a very pronounced increase in proliferation and interferon .gamma. (IFN-.gamma.) prodn. Exogenous IL-12 did not affect the B7-induced proliferation of naive T cells. Thus, whereas costimulatory signals delivered via B7-CD28 interaction are sufficient to induce significant proliferation of naive T cells activated through occupancy of the T cell receptor, Th1 T cell clones require cooperative costimulation by B7 and IL-12. This costimulation was shown to be specific by inhibition of proliferation and IFN-.gamma. prodn. using chimeric sol. cytolytic T lymphocyte-assocd. antigen 4-human IgG1Fc (CTLA4-Ig) and anti-IL-12 antibodies. Furthermore, the significant antigen specific proliferation and IFN-.gamma. prodn. by Th1 clones obsd. when splenocytes were used as APC was almost completely abrogated using CTLA4-Ig and anti-IL-12 antibodies. Thus two costimulatory signals, B7 and IL-12, account for the ability of splenic APC to induce maximal stimulation of Th1 clones. IL-10 down-regulates the expression of IL-12 by IFN-.gamma.-stimulated macrophages and this may account largely for the ability of IL-10 to inhibit APC function of splenic and macrophage APC for the induction of Th1 cell proliferation and IFN-.gamma. prodn. Indeed IL-12 can overcome the inhibitory effect of IL-10 for the APC-dependent induction of proliferation and IFN-.gamma. prodn. by Th1 clones. These results suggest that proliferation by terminally differentiated Th1 clones, in contrast to naive T cells, requires stimulation via membrane-bound B7 and a cytokine, IL-12. It is possible that these signals may result in the activation of unresponsive T cells during an inflammatory response. IL-10, by its role in regulating such innate inflammatory responses, may thus help to maintain these T cells in an unresponsive state.

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FILE 'USPATFULL' ENTERED AT 10:11:09 ON 12 NOV 1998
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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 10 Nov 1998 (19981110/PD)

FILE LAST UPDATED: 11 Nov 1998 (19981111/ED)
HIGHEST PATENT NUMBER: US5836014
CA INDEXING IS CURRENT THROUGH 11 Nov 1998 (19981111/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 10 Nov 1998 (19981110/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: May 1998
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 1998

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> > > (IPC) Manuals, editions 1-6, in the /IC1, /IC2, /IC3, /IC4, < < <
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> > > terms from the IPC subject headings and subheadings. < < <

This file contains CAS Registry Numbers for easy and accurate substance identification.

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ENTERED AT 09:23:48 ON 12 NOV 1998

L1 2 S 499E9
L2 222656 S (TNF OR TUMOR(W)NECROSIS(W)FACTOR)
L3 10817 S L2 AND (APOPTOSIS OR PROGRAMMED(W)CELL(W)DEATH)
L4 1973 S L3 AND LIGAND
L5 23 S L4 AND TH1(4A)CELL
L6 10 DUP REM L5 (13 DUPLICATES REMOVED)
E GORMAN DANIEL M/AU
L7 20 S E3 OR E2
L8 20 DUP REM L7 (0 DUPLICATES REMOVED)
E MATTSON JEANINE D/AU
L9 6 S E2 OR E3
L10 6 DUP REM L9 (0 DUPLICATES REMOVED)

FILE 'USPATFULL' ENTERED AT 10:11:09 ON 12 NOV 1998

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2764 TNF
69 TNFS
2774 TNF
(TNF OR TNFS)
19636 TUMOR
13907 TUMORS
23784 TUMOR
(TUMOR OR TUMORS)
7577 NECROSIS
1 NECROSISES
7578 NECROSIS
(NECROSIS OR NECROSISES)
257017 FACTOR
230954 FACTORS
404016 FACTOR
(FACTOR OR FACTORS)
2426 TUMOR(W) NECROSIS(W) FACTOR
546 APOPTOSIS
104226 PROGRAMMED
217003 CELL
175438 CELLS
259362 CELL
(CELL OR CELLS)
20385 DEATH
3829 DEATHS
22577 DEATH
(DEATH OR DEATHS)
284 PROGRAMMED(W) CELL(W) DEATH
19953 LIGAND
15985 LIGANDS
24886 LIGAND
(LIGAND OR LIGANDS)
1631 TH1
217003 CELL
175438 CELLS
259362 CELL
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95 TH1(4A) CELL
L11 2 L4 AND TH1(4A) CELL

=> d l11 1-2 ibib ab

L11 ANSWER 1 OF 2 USPATFULL
ACCESSION NUMBER: 1998:9379 USPATFULL
TITLE: Chimeric receptor molecules for delivery of co-stimulatory signals
INVENTOR(S): Roberts, Margo R., San Francisco, CA, United States
PATENT ASSIGNEE(S): Cell Genesys, Inc., Foster City, CA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5712149	980127
APPLICATION INFO.:	US 95-383749	950203 (8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Ulm, John
LEGAL REPRESENTATIVE: Sughrue, Mion, Zinn, Macpeak & Seas, PLLC
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1722
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to novel chimeric co-stimulatory receptor proteins and DNA sequences encoding these proteins. The chimeric receptors comprise at least three domains in a single chain molecule: an extracellular ligand binding domain, a transmembrane domain and a cytoplasmic co-stimulatory effector function signaling domain that acts synergistically with an effector function signal in the host cell. Novel hybrid co-stimulatory receptor proteins include a second cytoplasmic effector function signaling domain. The invention further relates to expression cassettes containing the nucleic acids encoding the novel chimeric receptors, to host cells expressing the novel chimeric receptors and to methods of using the receptors to co-stimulate effector functions in the cells and for using cells expressing the receptors for treatment of cancer, disease and viral infections.

L11 ANSWER 2 OF 2 USPATFULL

ACCESSION NUMBER: 97:104313 USPATFULL

TITLE: Chimeric receptor molecules for delivery of co-stimulatory signals

INVENTOR(S): Roberts, Margo R., San Francisco, CA, United States

PATENT ASSIGNEE(S): Cell Genesys, Inc., Foster City, CA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5686281	971111
APPLICATION INFO.:	US 95-455860	950531 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 95-383749, filed on 3 Feb 1995

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Ulm, John

LEGAL REPRESENTATIVE: Sughrue,Mion,Zinn,Macpeak & Seas, PLLC

NUMBER OF CLAIMS: 11

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 5 Drawing Figure(s); 3 Drawing Page(s)

LINE COUNT: 1627

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to novel chimeric co-stimulatory receptor proteins and DNA sequences encoding these proteins. The chimeric receptors comprise at least three domains in a single chain molecule: an extracellular ligand binding domain, a transmembrane domain and a cytoplasmic co-stimulatory effector function signaling domain that acts synergistically with an effector function signal in the host cell. Novel hybrid co-stimulatory receptor proteins include a second cytoplasmic effector function signaling domain. The invention further relates to expression cassettes containing the nucleic acids encoding the novel chimeric receptors, to host cells expressing the novel chimeric receptors and to methods of using the receptors to co-stimulate effector functions in the cells and for using cells expressing the receptors for treatment of cancer, disease and viral infections.

=> s l7

0 "GORMAN DANIEL M"/AU

1 "GORMAN DANIEL"/AU

L12 1 "GORMAN DANIEL M"/AU OR "GORMAN DANIEL"/AU

=> d l12 ibib ab

L12 ANSWER 1 OF 1 USPATFULL

ACCESSION NUMBER: 90:7518 USPATFULL

TITLE: Instrumentation column for the core of a pressurized water nuclear reactor

INVENTOR(S): Planchard, Jacques, Fontenay-aux-Roses, France
Godon, Jean-Luc, Paris, France
Gorman, Daniel, Ottawa, Canada
Gary, Gerard, Saint Cheron, France

PATENT ASSIGNEE(S): Electricite de France Service National, Paris, France (non-U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 4897239	900130
APPLICATION INFO.:	US 87-131207	871210 (7)

	NUMBER	DATE
PRIORITY INFORMATION:	FR 86-17419	861212

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Jordan, Charles T.

ASSISTANT EXAMINER: Wendtland, Richard W.

LEGAL REPRESENTATIVE: Pearne, Gordon, McCoy & Granger

NUMBER OF CLAIMS: 2

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 4 Drawing Figure(s); 3 Drawing Page(s)

LINE COUNT: 194

AB In a pressurized water nuclear reactor, the neutron flux is measured by introducing a probe into a glove finger tube, whose end is normally located in the reactor core. Each glove finger tube passes into a vertical instrumentation column, which is terminated by a nozzle (124) below one of the core assemblies. A clearance is provided around the glove finger tube in order to permit the outflow of cooling water from the core. To prevent vibration of the tubes level with nozzles (124), the latter are traversed by a passage (124a) having a constant diameter over most of its length and up to an upper planar face (124b).

=> s l9

0 "MATTSON JEANINE"/AU

0 "MATTSON JEANINE D"/AU

L13 0 "MATTSON JEANINE"/AU OR "MATTSON JEANINE D"/AU

=> d his

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FILE 'MEDLINE, CANCERLIT, SCISEARCH, BIOSIS, CAPLUS, EMBASE, WPIDS'
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L1 2 S 499E9

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L9 6 S E2 OR E3

L10 6 DUP REM L9 (0 DUPLICATES REMOVED)

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L11 2 S L5

FILE 'CAPLUS' ENTERED AT 10:14:50 ON 12 NOV 1998

FILE 'USPATFULL' ENTERED AT 10:14:51 ON 12 NOV 1998

L12 1 S L7

L13 0 S L9

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